GRB980425/SN1998bw (Fig. 1) that signals a strong connection between the two phenomena. The light curve of GRB030329, as discussed by Price *et al.*[2], shows a steepening that they interpret as being caused by a broadening of the jet-like outflow from its progenitor. The light curve also contains a wealth of other, finely structured detail that has interesting implications for the identity of the central engine driving the GRB. Uemura *et al.*[1] have found numerous bumps in the optical light curve, whose relative duration remains approximately constant, and at each of which the normalization of the light curve moves up (Fig. 1 on page 843). Simple explanations — that a jet has encountered an inhomogeneous, blobby medium or is itself patchy — do not work. But there is a satisfactory explanation[11]: as the leading edge of fast jet gas moves further away from the central engine of the burst, it starts to decelerate and is caught up by batches of slower-moving jet gas, creating a 'refreshed shock'[12]. These slower batches of gas could have been ejected towards the end of the γ-ray-emitting period (which lasts tens of seconds); at each catch-up episode, more energy is added to the afterglow.

The detection of GRB030329 is a watershed event. It proves that some, if not all, long GRBs are definitely associated with core-collapse supernovae, and thus are a consequence of the evolution of massive stars. It also strengthens the interpretation that the variability of burst light curves over short timescales is caused (largely, if not exclusively) by variable input from the central engine, rather than by the γ-rays encountering a variable external medium. These observations fill in important missing gaps in the phenomenology of GRBs.

But other questions have not been addressed, such as what the magnetic content of the jets[13] is, or whether all long bursts are associated with supernovae. Also, what is the connection between GRBs and the related, but fainter and softer phenomenon of X-ray flashes? The identity of the progenitors of the short GRBs is also an open question (a candidate might be mergers of double neutron stars), but it may be addressed by the Swift mission[14], to be launched this December. From the present observations[1–3] and their interpretation, however, it is clear that a new plateau has been reached in our understanding of the GRB phenomenon. ■

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Genome biology

Tales of the Y chromosome

Huntington F. Willard

Determining the sequence of the human Y chromosome presented a daunting challenge to genome researchers. But the task is now done, and the secrets revealed justify the effort.

Ancient maps showed the known world in colourful detail, beyond the edges of which lay vast expanses of *terra incognita*. Much creative thought went into portraying this unexplored territory, often featuring nasty-looking serpents and dragons. Only when Magellan managed to circumnavigate the globe did it become apparent that the unknown was in fact navigable, and that the serpents and dragons, if not illusory, could at least be tamed. The human genome has its *terra incognita* too, some of it known, much of it subject to alternating angst and fascination by genome biologists, and all of it to be avoided if possible — until now. On pages 825 and 873 of this issue[1,2], a group of modern-day Magellans describe how they sailed headlong into the frothy seas of duplicated, inverted and otherwise troublesome sequences on the human Y chromosome. They have emerged safely on the other side, with tales to tell.

Because of its distinctive role in sex determination, the Y chromosome has long attracted special attention from geneticists, evolutionary biologists and even the lay public. It is known to consist of regions of DNA that show quite distinctive genetic behaviour and genomic characteristics. The two human sex chromosomes, X and Y (Fig. 1), originated a few hundred million years ago from the same ancestral autosome — a non-sex chromosome — during the evolution of sex determination[3]. They then diverged in sequence over the succeeding aeons. Nowadays, there are relatively short regions at either end of the Y chromosome that are still identical to the corresponding regions of the X chromosome, reflecting the frequent exchange of DNA between these regions ('recombination') that occurs during sperm production[4]. But more than 95% of the modern-day Y chromosome is male-specific, consisting of some 23 million base pairs (Mb) of euchromatin — the part of our genome containing most of the genes — and a variable amount of heterochromatin, consisting of highly repetitive DNA and often dismissed as non-functional. Now, in an accomplishment that can only be described as heroic, Skaletsky *et al.*[1] report the complete sequence of the 23-Mb euchromatic segment, which they designate the MSY, for 'male-specific region of the Y'.

Prioritization in the Human Genome Project had led to the heterochromatic regions of the Y and other chromosomes being set aside to be dealt with later, if ever. But there was reason to hope that the euchromatin of the Y chromosome would present no more difficult a sequencing challenge than that found elsewhere in the genome. That supposition could not have been more wrong. As Skaletsky *et al.* report, the MSY is a mosaic of complex and interrelated sequences that made this one of the most problematic regions of the human genome thus far to be successfully sequenced and assembled.

For instance, about 10–15% of the MSY consists of stretches of sequence that moved there from the X chromosome within only the past few million years. These stretches are still 99% identical to their X-chromosome counterparts and are dominated by a high proportion of interspersed repetitive sequences, with only two genes. A further 20% of the MSY consists of a class of sequences ('X-degenerate' sequences[1]) that are more distantly related to the X chromosome, reflecting their more ancient common origin. And the remainder comprises a web of Y-specific repetitive sequences that make up a series of palindromes — sequences that read the same on both strands of the DNA double helix, with two 'arms' stretching out from a central point of mirrored symmetry. These palindromes come in a range of sizes, up to almost 3 Mb in length, with more than 99.9% identity between the two arms of each palindrome.

The repetitive sequences, particularly the palindromes, caused some difficulties for sequence assemblers. Genome-sequencing projects involve fragmenting the genome in question into small, overlapping pieces, sequencing them, and then using computer algorithms to put the pieces together in the correct order. There are various ways of doing this; assembling the MSY's palindromes (and discriminating between their arms) required an iterative mapping and

A. SYRED/SPL

Figure 1 **Male make-up. The human X (left) and Y chromosomes, magnified about 10,000 times.**

sequencing process more reminiscent of the knowledge-based mapping approaches of the early days of the Human Genome Project than the high-throughput assemblies that have emerged for most of the genome[5,6]. This strategy was aided by the fact that the sequence came from a single Y chromosome, so Skaletsky *et al.* knew that minor sequence variations must have come from duplicated copies on the same chromosome, rather than from different Y chromosomes. Although necessarily more painstaking, this overall approach provides a model for how researchers might attack at least some of the troublesome areas of the rest of the genome — such as blocks of repetitive heterochromatin and the hundreds of regions of substantial sequence duplication[7] — where standard assembly programs can be fooled.

This is not just a celebratory tale of a successful sequencing journey, however. Along the way, Skaletsky *et al.* picked up artefacts of Y-chromosome antiquity, dating as far back as 300 million years, that allow a glimpse into the evolutionary strategies that the Y chromosome has used to survive.

For instance, from the degree and patterns of divergence of the genes found on both sex chromosomes, the authors provide evidence for the stepwise decay of the Y chromosome over time and define changes in both Y-chromosome organization and gene content and expression. Unlike the regions at the ends, most of the lengths of the sex chromosomes do not exchange sequence during sperm production, and Skaletsky *et al.* point to two consequences of this suppression of recombination. First, selection occurred on the Y chromosome for a group of testis-specific genes that the authors argue may have enhanced male fertility. Most of these genes are found within the palindromes, showing why it can be important to sequence such difficult regions. Second, as X–Y recombination became suppressed during evolution, an alternative mechanism had to emerge to maintain the sequence and function of the remaining Y-chromosome genes and to prevent the accumulation of inactivating mutations and the ultimate demise of the chromosome[8].

To gain insight into this alternative mechanism, Rozen *et al.*[2] examined the hypothesis that X–Y recombination has been replaced by extensive, ongoing recombination between the arms of the MSY palindromes — where the sequence on one arm of the palindrome alters or ‘converts’ the sequence on the other. To test the predictions of this model, the authors sequenced one particular palindrome-embedded gene from Y chromosomes from around the world, representing the full tree of the previously established Y-chromosome genealogy[9]. They found several instances where the sequence of the copy of the gene on one arm of the palindrome had altered the sequence of the other arm’s copy. From this, they calculate that as many as 600 base pairs (from the 5.4 Mb contained in MSY palindromes) must be converted in each newborn male in the human population.

These data also indicate that gene conversion in general may be more common than previously suspected, especially in other palindromic and duplicated regions around the genome[7]. This supports a more dynamic view of genome change, in which, even within a single generation, not only does the occasional mutation occur (there are estimated to be as many as 100–200 new base-pair changes in each person), but also perhaps thousands of gene-conversion events.

The tales told by these Magellans of the genome hold two lessons for those who

100 YEARS AGO

May I record the discovery of musical sands at places along the shore between Ramsgate and Kingsgate. The sand occurs in small patches close to the chalk cliffs, the largest patch being found at Joss Gap. In composition the sand is very similar to that of Studland Bay, but the individual grains are more polished, and the proportion of denser materials far higher. Of course, the sand can only be experimented upon when it has been uncovered by the sea for a sufficient length of time to enable it to become dry, and it gives remarkable results when tested in the ordinary way — especially when placed in a china vessel and struck with a wooden plunger.

ALSO...

During a heavy thunderstorm at Heppner, Oregon, on Sunday last, a remarkable downpour of rain occurred, producing a destructive flood, which caused the death of more than three hundred people. Heppner is situated in a gulch through which a stream runs usually only a few feet in width. On Sunday a dense cloud suddenly covered the mountain overlooking the town, and the rain which followed produced a great mass of water which rushed down the mountain and carried everything before it… The flood swept a clean path more than a mile long and two blocks wide through the town.

From *Nature* 18 June 1903.

50 YEARS AGO

Interesting observations on the X-rays accompanying μ-meson capture by nuclei are reported through the rather unusual channel of a ‘press release’ from Columbia University. Negative μ-mesons brought to rest in matter eventually disappear, either by spontaneous decay or by nuclear capture… First the meson is attracted into quantum orbits around a nucleus, to which it is bound by the electrical forces. During this stage it emits X-rays or ejects atomic electrons as it jumps successively from one quantum state to another, until it reaches the state of lowest energy. Disintegration or capture then occurs… Rainwater and Fitch have observed these X-rays and made precise determinations of their energies. Since the deepest meson orbit and the nucleus are comparable in size for a heavy nucleus, the energy of the former is strongly influenced by the way in which electric charge is distributed in the nucleus… Rainwater and Fitch conclude that the charge is considerably more concentrated towards the centre than had been previously believed.

From *Nature* 20 June 1953.

might question the wisdom of such exploration. First, even the most repetitive and seemingly impenetrable stretches of the genome hold secrets that justify the effort. Second, each chromosome has its own story to tell, quite apart from the story of the genome as a whole. Although the sex chromosomes provide the strongest case for a special relationship between genome organization and the unique biology of a chromosome[10,11], the other chromosomes shouldn't feel left out. Each is the product of hundreds of millions of years of evolution, shaped by processes that have rearranged and exchanged sequences, contributed to the formation of new species, given birth to new genes and gene families, and provided the basis for a range of genetically determined or genomically influenced traits. Piecing together these events remains a worthwhile challenge, for among the flotsam and jetsam of each chromosome lie clues to our history. ■

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Global change

Ups and downs in the Red Sea

Frank Sirocko

Changes in past conditions in the Red Sea have been exploited to provide a detailed record of sea-level variation over much of the last glacial period. That record might tie in with events in the far south and north.

On page 853 of this issue, Siddall *et al.*[1] present a new approach to reconstructing the history of sea-level change during the last glacial cycle. They provide a detailed record, with a resolution on the century scale, spanning the years between 70,000 and 25,000 years ago. This was a time of intense overall glaciation, punctuated by abrupt warmings and coolings. The last glacial cycle culminated some 18,000 years ago with the so-called Last Glacial Maximum, before leading into our present interglacial condition, beginning about 10,000 years ago. The reason why past sea levels are of such interest is that they reflect global temperatures — during colder episodes, more of Earth's water becomes locked up in ice caps, with a consequent fall in sea levels.

The authors' approach involved analysing oxygen-isotope values of the calcite tests of foraminifera from Red Sea sediment cores. Foraminifera are planktonic organisms that originally lived in the surface waters, and accumulated calcite in equilibrium with an oxygen-isotope measure (δ^{18}O) of the water in which they lived. The δ^{18}O composition of the Red Sea is unlike that of the world ocean, because in this semi-enclosed basin the water is subject to especially strong evaporation. Strong evaporation favours release of the lighter ^{16}O isotope over that of ^{18}O — the water is thus enriched in ^{18}O, and is more saline.

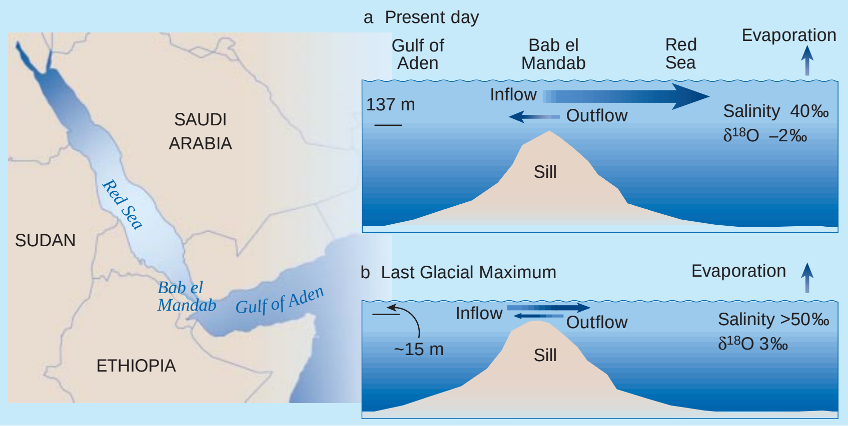

Figure 1 **Now and then at the Strait of Bab el Mandab, which is connected to the Indian Ocean through the Gulf of Aden.** a, **Status at the present day, during an interglacial with a water depth of about 137 m at the sill. Typical water conditions are a salinity of 40 parts per thousand (‰) and a δ^{18}O value of −2‰. In reality, the modern seasonal pattern of water flow is highly complex[4].**
b, **Status about 18,000 years ago, during a time of greatest cooling at the Last Glacial Maximum, with a water depth of approximately 15 m at the sill. The altered water-flow pattern and relatively stronger evaporative effect produced a salinity of more than 50‰, and a δ^{18}O value of 3‰. The size of the arrows is proportional to the strength of the processes indicated.**

This process is also typical for some other ocean basins at low latitude, such as the Persian Gulf or the Mediterranean. But the Red Sea is unique in the characteristics of its connection to the open ocean, through the Gulf of Aden. This connection, the Strait of Bab el Mandab, is only 18 km wide. It also has a 'sill', which at present lies 137 m below the surface. During the 'low stand' of sea level at the Last Glacial Maximum, however, it was at a depth of only about 15 m (Fig. 1). Accordingly, during glacial times, the amount of surface water flowing into the Red Sea was usually very restricted. The residence time of water in the basin was therefore much longer then than now, leading to an even greater evaporative effect on the δ^{18}O and salinity characteristics. Put another way, compared with that of other records, the sea-level signal seen in the Red Sea sediments is greatly amplified.

Siddall *et al.*[1] have combined a hydraulic control model[2] of water flow with an algorithm to calculate the equilibrium δ^{18}O values; these are a function of the composition of the inflowing water, the surface-water temperature, evaporation and the amount of inflow. The authors then applied this model to interpret the record of a sediment core, known as KL11, from the central Red Sea. The overall result is a history of sea level that shows several prolonged maxima and minima, especially between 70,000 and 40,000 years ago (see Fig. 2b, overleaf).

The broader significance of this work lies in how it might be related to the ice-core records at high latitudes, both south and north. Thus, the calculated salinities and model-derived sea levels show a succession of highs and lows that are similar to the temperature variations inferred from two Antarctic ice cores, Byrd and Vostok. The KL11 record shows for the first time that the temperature variations documented for the Antarctic were probably paralleled by changes in sea level (Fig. 2a, b).

A few years ago, the Byrd ice core was synchronized in time to the Greenland ice core, GISP2. To do this, the authors concerned[3] matched variations in levels of atmospheric methane, which must have occurred simultaneously worldwide. After carrying out this exercise, their most astonishing observation was that climate change in the Antarctic apparently occurred several millennia before